Talking Turkey and Tryptophan

November 23, 2005 -- In a classic episode of the TV sitcom, *Seinfeld*, Jerry is dating a woman whose father bequeathed her a collection of vintage toys, displayed in their original packaging on a bookcase in her living room. But she won't let Jerry, the eternal man-child, play with any of the toys. So he hits on an ingenious solution: feed her a heavy turkey dinner so that she falls into a deep sleep after the meal, leaving him free to explore the collection.

We've all encountered the myth that a heavy turkey dinner on Thanksgiving leads to inordinate sleepiness and the need for a cozy post-meal nap. It's usually attributed to the effects of **tryptophan**, an amino acid found in turkey and many other foods. In reality, **tryptophan's** effects can only be felt when ingested on an empty stomach, so a big turkey dinner isn't the best delivery mechanism for a sleep-inducing dosage.

However, there is growing scientific evidence that the amino acid does play a vital role in sleep and mood control, and it may even play a pivotal role in the immune system, according to Lawrence Steinman, a professor of neurology and neurological sciences who chairs the immunology program at Stanford University.

Tryptophan breaks down into at least four so-called metabolites. One is metatonin, which can lead to sleepiness. Another is serotonin, a mood-regulating substance that can be found in most antidepressants, such as Prozac. **Tryptophan** also breaks down into niacin (vitamin B3), and into a fourth class of product that is responsible for quieting down the immune system. It's that last metabolite that Steinman finds so intriguing, because of its potential to alleviate the symptoms of auto-immune diseases like multiple sclerosis.

Multiple sclerosis is a progressive disease in which the immune

system becomes overactive and launches an attack against the fatty cells that protect neurons, nerve cells called neurons that gather and transmit electrochemical signals, much like the gates and wires in a computer. More than 2.5 million people worldwide suffer from some variety of MS-related neurological disorder. One of the drugs used to treat MS in clinical trials overseas is an immuno-suppressant called **tranilast**, a synthetic **derivative** of **tryptophan** that quiets down an overactive immune system. Steinman discovered that **tranilast** is chemically very similar to metabolized **tryptophan**.

Steinman collaborated with a German postdoctoral researcher named Michael Platten to apply **tranilast** to models of MS using the cells of mice. They performed a series of experiments to determine the effects of four major **tryptophan** metabolites as well as **tranilast**. They found that all of the chemicals alleviated the symptoms of mice suffering from the mouse model of MS. And when they injected those mice with immune cells from other mice that had been protected from the disease with treatment using **tryptophan** metabolites, they could transfer that protective effect. This has important implications for effective treatments in human subjects to trigger regulatory T-cells, which suppress immune response instead of activating it.

The next step is to fund and organize a controlled clinical trial under the auspices of the Food and Drug Administration to test the effectiveness of **tryptophan** and trinilast on various auto-immune diseases. The breakdown products of **tryptophan** can increase the rate of cell death, which is a benefit in an overactive immune system, but can be a detriment to the central nervous system. "Like all drugs, [this] is a double-edged sword; there's a good side and a bad side," says Steinman. "We have to learn how and when to use it, and how large a dose is safe. Those are going to be tough questions."

"The bigger message here is that diet and immunity are inextricably linked," says Steinman, although the intersection between the two has not been extensively studied. "Now we have this very interesting science that ties trinilast up with **tryptophan**, underscoring the remarkable effect diet can have on immunity."

But Steinman is quick to point out that this doesn't mean we should all rush out to the nearest health food store to stock up on **tryptophan** supplements to help us sleep better, or to boost our immune systems -- precisely because so little scientific information is available on the practical benefits of doing so. So should we opt instead for eating more foods rich in **tryptophan**? This would include chicken, which actually contains more **tryptophan** than turkey. Not necessarily, says Steinman. For starters, one must be in an advanced stage of starvation for it to be truly effective; otherwise the **tryptophan** won't break down and will simply be absorbed into a protein.

"Even though many of the things we study in the lab, like **tryptophan**, modulate the immune system, are there practical things you can do in your diet to make a difference?" Steinman asks rhetorically. "My answer to that is, 'I don't know.'"

At left: President George W. Bush pardons a turkey named Marshmallow for Thanksgiving 2005.

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